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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,999	03/16/2001	David M. Neville	14028.0284U2	7991

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

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14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/810,999	Applicant(s) Neville et al.
	Examiner G.R. Ewoldt	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 12, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 4-8, 10, 12, and 13* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 4-8, 10, 12, and 13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5, 7, 9*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election of the species: methods of treating Type I diabetes, in Paper No. 13, filed 3/12/03, with traverse, is acknowledged. Applicant argues that a reasonable number of species are allowed under 37 CFR 1.141 and that no search burden has been established because Type I and Type II diabetes are "closely related pathologies".

Applicant is advised that on the finding of the allowability of a generic claim, all claims drawn to dependent species will be rejoined. Thus, a reasonable number of species would be allowed and the requirements under 37 CFR 1.141 would be satisfied. Regarding the asserted "closely related" nature of Type I and Type II diabetes, this assertion has not been established as fact. Type I diabetes is generally considered to comprise an actual loss of insulin-producing islet cells through an autoimmune process, whereas Type II diabetes is generally considered to comprise insulin resistance developed over time through unknown metabolic processes. It is also well-known that the diseases generally affect different patient populations, i.e., pre-teen and teen patients for Type I diabetes versus middle-aged and older patients for Type II diabetes. Accordingly, Applicant's assertion that "the same art must be searched for either Type 1 or Type 2 diabetes" is not scientifically accurate as significant differences between the diseases are known to exist.

The requirement is still deemed proper and is therefore made FINAL.

2. Claim 3 is withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b) as being drawn to a nonelected species.

Claims 1, 2, 4-8, 10, 12, and 13 are being acted upon.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 2, 4, 10, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for the treatment of diabetes comprising the administration of UCHT1-CRM9, an immunosuppressant, and pancreatic islet cells from a donor,

does not reasonably provide enablement for:

a method for the treatment of diabetes comprising the administration of an immunotoxin, an immunosuppressant, and pancreatic islet cells from a donor.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding a treatment for diabetes, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable. The state of the medical art is such that no immunomodulatory/transplant methods are currently available for the effective treatment of diabetes.

The specification provides insufficient data to enable claims drawn to the method as broadly claimed. Note that the method encompasses the use of *any* immunotoxin, whereas the specification discloses a method wherein the immunotoxin must be capable of depleting T cells. See, for example, Example 3; the example clearly discloses that an anti-CD5 immunotoxin was

incapable of reducing the number of T cells (thus, the immunotoxin could not function in the claimed method), therefore, the specification indicates that the method of the claims cannot function as claimed. Accordingly, the method as broadly claimed must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 2, 4-8, 10, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,103,235 (IDS).

The '235 patent teaches a method of administering the immunotoxin UCHT1-CRM9 (the anti-CD3-CRM9 immunotoxin of Neville et al., J. *Biol. Chem.*, 1989, column 5, lines 61-62), deoxyspergualin (column 8, line 51), and pancreatic islet cells (column 9, line 44).

The reference teaching differs from the claimed invention only in that it does not teach the method for the treating of diabetes however, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention to perform the method for the treating of diabetes as this was the most common disease for which pancreatic islet cell transplantation would have been used as a treatment. Further, the timing of said administration (such as is set forth in Claims 10 and 12) comprises only routine optimization of the claimed method. Said routine optimization would fall well within the purview of one of skill in the art at the time of the invention.

7. Claims 1, 2, 4-8, 10, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/32137 (1996, IDS), in view of Henretta et al. (1994, IDS).

WO 96/32137 teaches the administering the immunotoxin UCHT1-CRM9 (the anti-CD3-CRM9 immunotoxin of Neville et al., J. *Biol. Chem.*) for T cell depletion, and the administration of an immunosuppressant, as a method of inhibiting a rejection response to the transplantation of pancreatic islet cells (page 18-19 and page 92). The reference further teaches that immunotoxins such as UCHT1-CRM9 are superior for T cell depletion in that they are capable of extreme depletion of a specific target type (such as T cells) (page 92).

The reference teaching differs from the claimed invention only in that it does not teach the use of the immunosuppressant deoxyspergualin, nor the use of said method for the treating of diabetes.

Henretta et al. teaches the use of T cell depletion and administering deoxyspergualin to prolong the survival of engrafted pancreatic islet cells as a treatment for diabetes.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention to perform the administration of the immunotoxin UCHT1-CRM9 (for T cell depletion) and the administration of an immunosuppressant, as a method of inhibiting a rejection response to the transplantation of pancreatic islet cells, as taught by WO 96/32137, specifically, as a method for the inhibition of pancreatic islet cell transplantation for the treating of diabetes and the use of deoxyspergualin as the immunosuppressant, as taught by Henretta et al. One of ordinary skill in the art would have been motivated to perform the combined method as a treatment of diabetes given the teachings of Henretta et al. that pancreatic islet cell transplantation along with T cell depletion and administering deoxyspergualin would prolong the survival of engrafted pancreatic islet cells as a treatment for diabetes. Note that the timing of said administration (such as is set forth in Claims 10 and 12) comprises only routine optimization of the claimed method. Said routine optimization would fall well within the purview of one of skill in the art at the time of the invention.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 at (703) 305-3014. The CM1 Fax Center telephone numbers are 703-872-9306 (before final) and 703-872-9307 (after final).

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600
May 19, 2003